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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,383	06/26/2006	Kyu Hyun Lee	5804900032	3667
Joseph Hyosuk Kim JHK Law P.O. Box 1078 La Canada, CA 91012-1078				
7590 05/28/2008			EXAMINER HIRIYANNA, KELAGINAMANE T	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 05/28/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/584,383

Applicant(s)

LEE ET AL.

Examiner

KELAGINAMANE T. HIRIYANNA

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01/17/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 01/17/2008 in response to office action mailed on 09/07/2007 has been acknowledged.

Claims 1-3, 8, 18, 20, and 21 are amended.

Claims 1-23 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

The Applicant's arguments and the declaration filed by one of the applicants under 37 C.F.R. § 1.132 on 01/17/2008 are duly considered while writing this office action.

Claim rejections under 35 U.S.C. 112, first paragraph (written description and enablement) has been withdrawn in view of applicants arguments and amendments to claims in the response of 01/17/2008.

Rejection of claims 1-4 and 8-10 under 35 USC 102 (b) as being anticipated by Chang et al., (WO 01/19868) has been withdrawn in view of applicant's amending the claims to read specifically on animal cells thus excluding said recombinant gene expression in bacterial cells and further in view of a 35 USC 103 rejection of the claims below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-23 stand rejected under 35 USC 103 (a) as being unpatentable over Chang et al (WO 01/19868 A1; art of record) in view of Trieu et. al (1999, Biochem. Biophys. Res. Comm. 257: 714-718; art of record).

The above claims are directed to a pharmaceutical composition containing a gene carrier or cell harboring human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) and in further limitations carrier is a vector or a recombinant virus and the cells harboring vector including hematopoietic stem cells, dendritic cells and to a method of for the prevention or the treatment of a solid tumor including its growth or metastasis by administering said gene carrier.

Regarding claims 1-4, and 8-10 Chang teaches compositions comprising vectors with nucleotide sequences SEQ ID NO: 1 or 2 encoding human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) (Abstract, p.1, lines 8-17, p.4, lines 27-36 bridging p.5). Chang further teaches that proteins encoded by said sequences as anticancer agents and inhibit angiogenesis (Abstract), p.3, lines 10-37 bridging p.4-5) and they inhibit endothelial cell proliferation, migration and suppress lung carcinoma (p.15, lines 10-35 bridging p.16-20). Chang however does not teach said nucleic acid compositions in animal cells and a method of treating tumors by administering said nucleic acids into any animal.

Regarding claims 1-4, 8-10 and 18-21 Trieu teaches that there is an established link between cancer and Apo(a) (the protein that contains KIV9-KIV10-KV (LK68) or KV (LK8)) levels and a method of treating Lewis lung carcinoma (LL/2) cancer wherein the cancer cells show a delayed growth of tumor and reduced angiogenesis when provided with apo(a) transgene (Abstract and entire article). Regarding claim 6 Trieu teaches providing CHO-K1 cells over expressing truncated human apo(a) transfected using a vector. Trieu further teaches full length recombinant apo(a) causes tumor suppression (p.714, abstract, col.2, 1st paragraph, 3rd paragraph; p.715, col.1 3rd paragraph, col.2, 1st paragraph; p.716, Fig.2). Trieu additionally teaches that a further characterization of structural components of apo(a) responsible for its previously unappreciated anti-tumor effects may provide the basis for novel and effective cancer treatment methods that employ apo(a) fragment or functional analogs of apo(a) as inhibitors of tumor

angiogenesis. Trieu however, does not particularly teach the limitation of using gene coding for Apo(a) protein fragments in vectors or gene carriers recited in instant claims.

Regarding limitations in claims 5, 7, 11-15, 22-23 of specific vectors used for methods of delivering and expressing said nucleic acid sequences in animal cells, prior art at the time of invention inherently and clearly teaches the use of several of the claimed vectors including viral vectors (for example see Kuo et al, 2001, PNAS 98:4605-4610; art of record) for delivering therapeutic genes into animal cells and for treating a solid tumor and metastasis thereof.

Thus it would have been obvious to one of skill in the art to substitute the full length apo(a) fragment in the gene therapeutic vector construct of Trieu or a viral vector described in prior art with a fragment of apo(a) gene that codes for LK68 and LK8 kringles and prepare a composition and treat a solid tumor or metastasis of thereof in an animal subject. One of the skill in the art would have been motivated to use the gene fragment that codes for LK68 and LK8 kringles in specific viral vector/or vector transfected as these gene carriers increase the efficacy of a tumor gene therapy. One of skill in the art would have an expectation of success of making and using a pharmaceutical composition for gene therapy of tumors using gene coding sequences for kringles KIV9-KIV10-KV (LK68) or KV (LK8) cloned in viral or non-viral vectors as the art at the time of invention teaches that sub-cloning of gene fragments in therapeutic vectors and their therapeutic use is routine. Further it would have been obvious to try using different vectors described in the art of tumor gene therapy to deliver and express LK68 and LK8 kringles. Thus the invention as claimed would have been *prima facie* obvious to one of skill in the art.

Response to Applicants arguments of 12/07/2007:

The applicant argues Chang et al., did not describe the use of gene carriers or vectors for expression in human or animal cells and Trieu et al does not teach that truncated fragments of apo(a) are effective against tumor angiogenesis and hence a combination of the above two references do not make the invention obvious over the existing prior art.

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The Applicants arguments however found not persuasive because in the first place the Applicant should note that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). As far as the motivation to combine the previously cited references and the relevant prior art Applicant should note Chang clearly teaches the tumor therapeutic efficacy of LK68 and LK8 as well as the cDNA sequences coding them where as Trieu clearly teaches the use of DNA sequences comprising said kringles in eukaryotic expression vectors for expressing in animal cells and for gene therapy. Thus combination of the teachings of the above references combined with the relevant prior art teachings regarding various vectors used in tumor gene therapy the instant invention would have been obvious to an artisan in the art. Hence the rejection is maintained.

Conclusion:

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanne Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanne

Patent Examiner

Art Unit 1633

/Robert M Kelly/

Acting Examiner of Art Unit 1633

Application Number**Application/Control No.**

10/584,383

**Applicant(s)/Patent under
Reexamination**

LEE ET AL.

ExaminerKELAGINAMANE T.
HIRIYANNA**Art Unit**

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